



PATENT
Attorney Docket No. 213257

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Kovesdi et al.

Application No. 09/964,065

Filed: September 26, 2001

Art Unit: 1632

Examiner: S.D. Priebe

RECEIVED

MAR 18 2003

For: REPLICATION-DEFICIENT ADENOVIRAL
VECTOR AND PLASMID WITH
ADENOVIRAL COMPONENT

TECH CENTER 1600/2900

PENDING CLAIMS AFTER AMENDMENTS
MADE IN RESPONSE TO OFFICE ACTION DATED DECEMBER 6, 2002

44. A plasmid comprising a reading frame ORF6 of an E4 region of an adenovirus genome under the control of a heterologous inducible promoter.

48. A defective recombinant adenovirus that (a) requires, for replication, complementation *in trans* of one or more essential gene functions of an E1 region and an E4 region of an adenovirus genome; and (b) comprises an adenoviral genome having a deficiency of one or more essential gene functions of the E1 region, a deletion of the entire E4 region, and optionally a deletion of all or part of the E3 region.

50. The defective recombinant adenovirus of claim 48, wherein the adenoviral vector comprises an adenoviral genome having a deficiency of all essential gene functions of the E1 region.

52. The defective recombinant adenovirus of claim 50, wherein all or part of the E3 region is deleted.

53. A system comprising:
(i) an adenoviral vector comprising an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome, and optionally a deficiency in the E3 region of the adenoviral genome, and

(ii) a cell having a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome,

wherein there is no overlap between the cellular genome and the adenoviral genome to mediate a recombination event between the cellular genome and the adenoviral genome.

54. The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

55. The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of the E4 region of the adenoviral genome, and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of the E4 region of the adenoviral genome.

56. The system of claim 55, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

57. The system of claim 55, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

58. The system of claim 57, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

59. The system of claim 57, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

60. The system of claim 59, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

63. A method of propagating an adenoviral vector, which method comprises

- (a) providing an adenoviral vector comprising an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome, and optionally a deficiency in the E3 region of the adenoviral genome,
- (b) providing a cell comprising a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome, wherein there is no overlap between the cellular genome and the adenoviral genome to mediate a recombination event between the cellular genome and the adenoviral genome, and
- (c) propagating the adenoviral vector in the cell.

64. The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

65. The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of the E4 region of the adenoviral genome, and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions in the E4 region of the adenoviral genome.

66. The method of claim 65, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and

the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

67. The method of claim 65, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

68. The method of claim 67, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

69. The method of claim 67, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

70. The method of claim 69, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

73. The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of the E2A region of the adenoviral genome, and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of the E2A region of the adenoviral genome.

74. The system of claim 73, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

75. The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of both the E2A region and the E4 region of the adenoviral genome and the cell has a cellular

genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of both the E2A region and the E4 region of the adenoviral genome.

76. The system of claim 75, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

77. The system of claim 75, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

78. The system of claim 77, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

79. The system of claim 77, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

80. The system of claim 79, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

81. The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of the E2A region of the adenoviral genome, and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of the E2A region of the adenoviral genome.

82. The method of claim 81, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and

the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

83. The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of both the E2A region and the E4 region of the adenoviral genome and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of both the E2A region and the E4 region of the adenoviral genome.

84. The method of claim 83, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

85. The method of claim 83, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

86. The method of claim 85, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

87. The method of claim 85, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

88. The method of claim 87, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

89. The defective recombinant adenovirus of claim 48, wherein the adenoviral genome is a human adenoviral genome.

90. The defective recombinant adenovirus of claim 89, wherein the adenoviral genome is an Ad5 adenoviral genome.

91. The system of claim 53, wherein the adenoviral genome is a human adenoviral genome.

92. The system of claim 91, wherein the adenoviral genome is an Ad5 adenoviral genome.

93. The system of claim 55, wherein the adenoviral genome is a human adenoviral genome.

94. The system of claim 93, wherein the adenoviral genome is an Ad5 adenoviral genome.

95. The method of claim 63, wherein the adenoviral genome is a human adenoviral genome.

96. The method of claim 95, wherein the adenoviral genome is an Ad5 adenoviral genome.

97. The method of claim 65, wherein the adenoviral genome is a human adenoviral genome.

98. The method of claim 97, wherein the adenoviral genome is an Ad5 adenoviral genome.